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Guangzhou Zou

1392/10/21 PCT/US

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06/20/2008

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EXAMINER

SKOWRONEK, KARLHEINZ R

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

06/20/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/500,587

Applicant(s)

ZOU ET AL.

Examiner

KARLHEINZ R. SKOWRONEK

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8-13, 15-27, 29 and 30 is/are pending in the application.
- 4a) Of the above claim(s) 15-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-13 and 29-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

It is noted that the last office action contained an error in the citation for the publication used in the rejection of claim 1-6 under 103(a). The rejection erroneously cited Wohlgemuth et al. (US PG PUB 2004/0009479), the citation should have been Wohlgemuth et al. (US PG PUB 2007/0037144) as noted correctly in the second rejection under 35 USC 103(a) and Notice of References Cited of the Office Action mailed 07 August 2007. The examiner regrets any inconvenience caused by the error.

Claim Status

Claims 1-6, 8-13, 15-27 and 29-30 are pending.

Claims 7, 14, and 28 are cancelled.

Claims 13-27 stand withdrawn as being directed to a non-elected invention.

Claims 1-6, 8-13, and 29-30 are being examined.

Specification

Response to Arguments

Applicant's arguments, see Remarks p. 9, filed 07 arch 2008, with respect to the objection to the specification for containing hyperlinks have been fully considered and are persuasive. The objection to the specification has been withdrawn in view of the amendment of the specification.

Claim Objections

Applicant's arguments, see Remarks p. 10, filed 07 March 2008, with respect to the objection to claim 14 have been fully considered and are persuasive. The objection of claim 14 has been withdrawn in view of the cancellation of claim 14.

Claim Rejections - 35 USC § 112

Response to Arguments

Applicant's arguments, see Remarks p. 10, filed 07 March 2008, with respect to the rejection of claim 1 under 35 USC 112, second paragraph as have been fully considered and are persuasive. The rejection of claim 1 has been withdrawn in view of the amendment to the claim.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 8-13, and 29-30 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-6, 8-13, and 29-30 drawn to a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). The instant

claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in *State Street Bank & Trust Co. v. Signature Financial Group Inc.* CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to -- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above, claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 1-6, 8-13, and 29-30 do not require production of a tangible result in a form that is useful to the user of the process or apparatus. The claims are directed to a method of correcting hybridization in which measured signals are subjected to a

correction coefficient calculation and outputted to a computer memory. The embodiment of outputting to a memory is not tangible to the practitioner of the process. That is, the user of the process in which the result is output to a memory would have a result that is not in form that the practitioner can interpret and apply. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment.

Response to Arguments

Applicant's arguments filed 07 March 2008 have been fully considered but they are not persuasive. Applicant argues that amendment of the claims to recite an output to a memory overcomes the rejection under 35 USC 101 as non-statutory by lacking a tangible output. The result of the method as currently claimed remains non-tangible to the user of the process, thus the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Pietu et al. (Genome Research, Vol. 6, p. 492-503, 1996).

The claims are directed to a method of correcting oligo probe hybridization signals in which signals of multiple hybridizations are measured, a correction coefficient is calculated for each probe such that the probe's average is equal to a constant, correct each probe signal with the correction coefficient and outputting the corrected signal.

Pietu et al. shows the analysis of hybridization signals from microarrays. Pietu et al. shows that signal intensities of multiple hybridizations are measured (p. 493, col. 2). Pietu et al. shows that each probe is divided by the average of all probes (p. 502, col.1). The correction of the signal intensity data in Pietu et al. reads on the limitations because Pietu et al. show each probe's intensity is corrected by a coefficient that is $1/(\text{average intensity})$, therefore if the average intensity is multiplied by the same coefficient the result is a constant, that is 1. This teaching reads on the limitation that each probe's signal is corrected using a coefficient such that the probe's average is equal to a constant. Pietu et al. show the probes' signal intensities are corrected and output (p. 502, col. 1). Pietu et al. shows the calculation of standard deviation and average (p.502, col. 2). Pietu et al. shows the determination of an uncertainty coefficient that is a ratio of the average to the standard deviation (p.502, col. 1).

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, see declaration under 37 CFR 1.131, filed 07 March 2008, with respect to the rejection(s) of claim(s) 1-6 as unpatentable over Jelinsky et al.

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in view of Wohlgemuth (US PG PUB 2004/0009479) under 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn in view of the declaration. However, upon further consideration, a new ground(s) of rejection is made in view of Wohlgemuth et al. (US PG PUB 2007/0037144).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wohlgemuth et al. (US PGPUB 2007/0037144).

The claims are directed to a method of correcting probe hybridization signals by measuring signals from each oligo probe in multiple hybridizations; calculating a correction coefficient for the probes such that the signal average is equal to a constant; and correcting the signal for the probes using the calculated correction coefficient. In some embodiments, an average and standard deviation for the signals observed for each probe are calculated. In some embodiments, an uncertainty coefficient, called signal to noise ratio, is calculated based on the ratio of the average to standard deviation.

Jelinsky et al. teach a method of correcting oligo probe hybridization signals (p. 8157, col. 2, para 2, line 1-22). Jelinsky et al. show that 4 arrays of 6218 probes each were incubated with 10ug RNA, washed and scanned (p. 8157, col. 2, para 2, line 2-6). Jelinsky et al. show that a correction coefficient is calculated for the arrays such that the average of the intensities on the array is equal to a constant, 300 (p. 8157, col. 2, line16-18). Jelinsky et al. teach that the scaling allows the arrays to be directly compared with each other (p. 8157, col. 2, line18-19).

Jelinsky et al. do not show the calculation of individual correction coefficients for individual probes where the average signal of the individual probes is made to equal a constant.

Wohlgemuth et al. show a method of measuring DNA hybridization. Wohlgemuth et al. teach individual probes or median background subtracted signals (BGSS) can be scaled to be between 0 and 1 [0212]. Wohlgemuth et al. teach that scaling is desirable because it has the advantage of facilitating the comparison of data between different experiments [0212]. Wohlgemuth et al. teach that DNA is genomic DNA [0091]. Wohlgemuth et al. show that an average and standard deviation for the signals observed for each probe are calculated [207]. Wohlgemuth et al. show that an uncertainty coefficient, called signal to noise ratio, is calculated based on the ratio of the average to standard deviation [0207]. Wohlgemuth et al. show that probes that do not have a certain predetermined signal to noise ratio are disregarded. In Wohlgemuth et al., the signal to noise ratio is calculated as mean divided by the standard deviation. The signal to noise ratio is the inverse of the coefficient of variation, standard deviation divided by the mean. Wohlgemuth et al. teach that if the signal to noise ratio is less than 3 which is equivalent to having a coefficient of variation that is greater than 0.33 the data is flagged but used, reading on a predetermined value that is approximately 1.0 [0728]. As the signal to noise ratio decreases, it approaches 1. When the signal to noise ratio is equal to 1, the ratio indicates that signal cannot be distinguished from the noise, indicative of data of poor quality. Similarly, for the inverse of the signal to noise ratio, coefficient of variation (CV), as the CV increases to approach 1, the quality of the data becomes poorer and less reliable. Wohlgemuth et al. teach that if a replicate feature is of poor quality it can be disregarded and the remaining features used to represent the gene [0200].

It would have been obvious to one of skill in the art to modify the method of correcting oligo probe hybridization signals of Jelinsky et al. with the individual probe scale factors of Wohlgemuth et al. because Wohlgemuth et al. shows that scaling provides the advantage of facilitating the comparison of data between different experiments. As the signal to noise ratio decreases, it approaches 1. When the signal to noise ratio is equal to 1, the ratio indicates that signal cannot be distinguished from the noise, indicative of data of poor quality. Similarly, for the inverse of the signal to noise ratio, coefficient of variation (CV), as the CV increases to approach 1, the quality of the data becomes poorer and less reliable.

The following rejection is reiterated from the previous action.

Claim 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wohlgemuth et al. (US PG PUB 2007/0037144) as applied to claims 1-5 above, and further in view of Pinkel et al. (US Pat 5,830,645).

The claims are drawn to determining a dynamic range for DNA binding.

Jelinsky et al. (Mol. Cell. Biol., Vol. 20, No. 21, p.8157-8167, November 2000), in view of Wohlgemuth et al. (US PG PUB 2007/0037144) as applied to claims 1-5 above do not teach determining a dynamic range for DNA binding.

Pinkel et al. show a method comparative genomic hybridization. Pinkel et al. show that the method provides increased sensitivity, more precise localization of chromosomal abnormalities and which can detect differences in levels of gene

expression are particularly desirable for the diagnosis of disease (col. 2, line 23-26). Pinkel et al. show that serial dilutions of pairs of fluorochrome in known relative proportions can also be analyzed to determine the accuracy with which fluorescence ratio measurements reflect actual fluorochrome ratios over the dynamic range permitted by the detectors and membrane fluorescence (col. 8, line 44-49).

It would have been obvious to one of skill in the art to modify the method of correcting oligo probe hybridization signals of Jelinsky et al., in view of Wohlgemuth et al. as applied to claims 1-5 above and in further view of the method comparative genomic hybridization by Pinkel et al. because Pinkel et al. show that Pinkel et al. show that the method provides increased sensitivity, more precise localization of chromosomal abnormalities and which can detect differences in levels of gene expression are particularly desirable for the diagnosis of disease.

Response to Arguments

Applicant's arguments filed 07 March 2008 have been fully considered but they are not persuasive. Applicant argues that the rejection is moot in view of the declaration under 37 CFR 1.131. This not persuasive because claims 8-14 were rejected over Wohlgemuth et al. (US PG PUB 2007/0037144) and not US PG PUB 2004/0009479. Wohlgemuth et al. (US PG PUB 2007/0037144) was filed on 22 October 2000 claims priority to two provisional applications the first dated 8 June 2001 and the second dated 20 October 2000. Applicant's declaration while sufficient to overcome the first priority document filed 8 June 2000, is insufficient to overcome the second earlier priority document. 20 October 2000 fell on a Friday, whereas 20 October 2001 fell on a

Saturday. In accordance with 37 CFR 1.6 and 35 USC 119(e)(3) the period of pendency of a provisional application is extended to the next business day if the day that is 12 months after the filing date of a provisional application falls on a Saturday, Sunday, or Federal holiday within the District of Columbia.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on Mon-Fri 8:00am-5:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

20 June 2008

/K. R. S./

Examiner, Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631